REMARKS

After entry of the complete listing of the claims provided above, claims now pending in this application include: 283-362, 364-380, 382-398, 400-404, 406-439, 441-508, 510-511, 516-525 and 527-549. Claims 516, 522 and 524 have been amended. Claims 509, 512-515 and 526 have been canceled. Two claims, 548 and 549, have been added by this paper. Entry of the above listing and claim amendments is respectfully requested.

Before addressing the claim amendments and the issues that were discussed at the August 12, 2004 interview, Applicants wish to express their gratitude for the courtesy and time extended by the Examiner to Applicants' representative, Eugene C. Rzucidlo, Esq. of the law firm, Greenberg Traurig, LLP, and their undersigned attorney.

I. Summary of August 12, 2004 PTO Interview

Using Applicants' May 28, 2004 Amendment Under 37 C.F.R. §1.115 as a reference point, the following matters were discussed at the interview:

A. Claim 510 (Page 82, 1st Full ¶)

The Examiner indicated that the amendments to claim 510 were acceptable. Claim 510 recites "[a] polynucleotide sequence covalently attached to a hormone."

B. Claims 512 & 524 (Page 82, 2nd Full ¶ and Page 83, 2nd Full ¶)

The Examiner indicated that he thought that the language in claims 512 and 524 did not find full support in the original claims, namely, original claim 78. In particular, he noted that original claim 78 recited a list of sequences followed by the phrase "and a repeating low-complexity polynucleotide." The Examiner added

that he thought that claims 512 and 524 should be amended to conform to the language in original claim 78. Applicants' attorney replied that he would probably submit amendments for both claims 512 and 524.

C. **Claims 513 and 520 (Page 82, last ¶, through Page 83, 1st ¶)**

The Examiner indicated that it is possible on the one hand to derive DNA from a filamentous phage, and on the other hand, to derive a filamentous phage from DNA. He inquired whether the former is the interpretation that should be given to amended claims 513 and 520. Applicants' attorney urged the interpretation that is given in the new language of claims 513 and 520, namely that the DNA molecule is derived from a filamentous phage. Applicants' attorney added that there was support for the phrase "wherein said DNA molecule is derived from a filamentous phage," and that the amendment was intended to clarify the subject matter being claimed. The Examiner and Applicants' attorney discussed the possibility that the amendment could be to correct an obvious error in the disclosure that is clear from its context. If so, the Examiner urged a statement to that effect.[2]

[2] Although not discussed at the August 12, 2004 interview, it is noted that footnote 2 on page 83 in Applicants' May 28, 2004 Amendment provided:

> See the original specification, page 16, lines 11-20; Example 32; and original claims 31, 32, 44, 45, 70 and 71 (DNA polymer or bridging entity "is *derived* from a filamentous phage").

The portions and claims listed above in footnote 2 would appear to provide the requisite support for the language in claims 513 and 520 with respect to the DNA molecule being derived from a filamentous phage. Please note, however, that claim 513 has been canceled above. See discussion below under II. Claim Amendments, Point 1, Cancellation of Claims 509, 512-515 and 526.

D. **Definiteness & Written Description for Claims 283 et al. (Page 87, through first half of page 88)**

With respect to the "binding" language in claim 283 and other claims[3], the Examiner indicated that he thought the amendments were acceptable.

E. **Claim 509 (Page 89, 1st full ¶)**

The Examiner inquired as to the support for the "non-nucleotidyl" recitation in claim 509 and 522.[4] Applicants' attorney indicated that he would respond to this query in their next supplemental response.

F. **Claims 512-517 and 520-527 (Page 89, last ¶)**

The Examiner indicated that he thought these claims were unclear due to the "low complexity" language. He also referred to some work in the 1980s by Dr. Alec Jeffreys on repeating nucleotide sequences that were not continuous. Applicants' attorney indicated that before submitting their supplemental response, Applicants would review the language in claims 512-517 and 520-527, in light of Maniatis's cited 1982 Molecular Cloning publication, and perhaps, Dr. Jeffreys's work to the extent it represented prior art to their present application.

G. **Claim 506 (Page 90, last ¶, through Page 91)**

The Examiner expressed concern that the language in claim 506 ["A polynucleotide sequence covalently attached to an antibody."] could still be

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[3] The other claims which were amended in response to the "binding" issue included claims 284-294, 360-361, 411-417, 434, 443-460, 464-487 and 546. See page 80, third full paragraph, in Applicants' May 28, 2004 Amendment.

[4] As amended by Applicants' May 28, 2004 Amendment, claim 509 recited "[a] polynucleotide sequence covalently attached to a non-nucleotidyl saccharide having up to 20 saccharide units." As also amended by that paper, claim 522 recited "[a] circular DNA molecule covalently attached to a non-radiolabeled non-nucleotidyl signal generating moiety." Please note that claim 509 has been canceled by this paper. See discussion below in II. Claim Amendments Point 1 Cancellation of Claims 509, 512-515 and 526.

covered by Langer et al.'s cited 1981 PNAS paper. He indicated that although the binding between biotin and avidin is non-covalent, the biotin molecule in Langer's disclosure is covalently attached to the polynucleotide. Hence, according to the Examiner, the avidin molecule could be seen or interpreted as being covalently attached to the polynucleotide through the intervening and covalently attached biotin molecule. Applicants' attorney disagreed with this statement and he indicated that the attachment of avidin to biotin is non-covalent, and that Langer did not disclose the covalent attachment of avidin to the polynucleotide. Although the Examiner and Applicants' attorney discussed some new language for claim 506, no agreement was reached. Applicants' attorney asked whether he might be able to fax to the Examiner some proposed language to claim 506, and the Examiner agreed to that suggestion.

This is the end of Applicants' summary of the August 12, 2004 interview.

II. Claim Amendments

1. *Cancellation of Claims 509, 512-515 & 526*

As noted above, claims 509, 512-515 and 526 have been canceled, thereby reducing the number of outstanding issues in this application.

2. *Claim 522*

Claim 522 has been amended to recite "[a] circular DNA molecule covalently attached to a non-radiolabeled signal generating moiety *capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent*

compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase. Support for the italicized portion above is found in the specification, beginning with page 18, last paragraph, and continuing through page 21.

It should be noted that the term "non-nucleotidyl" in claim 522 has been deleted in favor of the language italicized above. Although Applicants believe that their specification fully supports the former "non-nucleotidyl" recitation, they have deleted this term nevertheless in favor of the new language above. It is believed that the amendments to claim 522 also distinguishes Applicants' claimed invention from the documents cited of record in this application, including Maniatis's Molecular Cloning (1982) publication.

3. ***Claim 516 & 524***

Claim 516 has been amended above to recite "[a] DNA molecule which carries a polynucleotide sequence complementary to a gene sequence or portion thereof of a nucleic acid containing organism, and which further carries a polynucleotide portion which comprises a repeating low-complexity polynucleotide sequence of a dinucleotide repeat or a trinucleotide repeat." Formerly, this claim depended from claim 512, the latter having now been canceled. The first part of claim 516 reflects the earlier language in the claim with respect to carrying a polynucleotide sequence complementary to a gene sequence. The second part of claim 516 calls for a polynucleotide sequence which comprises a repeating low-complexity polynucleotide sequence of a dinucleotide repeat or a trinucleotide repeat. Claim 524 recites similar language as claim 516 with respect to the dinucleotide repeat and the trinucleotide repeat.

Support for the "repeating low-complexity polynucleotide sequence" in claim 516 and 524 is found on page 15, lines 6-13:

> . . . It is thus preferred to choose polynucleotide sequence portions on the bridging entity which are non-coding, and not likely to be complementary to sequences on the analyte such as, for example, ***sequences comprising poly deoxy G, poly deoxy A, poly deoxy GT, poly deoxy GA, poly deoxy GAT, poly deoxy GTA, or any other low complexity (repeating) sequence***. . . [emphasis added]

Applicants respectfully point out that in the portion quoted above the phrase "or any other low complexity (repeating) sequence" refers to the previously recited sequences (poly deoxy G, poly deoxy A, etc.). With respect to the "dinucleotide repeat" and the "trinucleotide repeat," these refer to such low-complexity (repeating) sequences having two or three nucleotides.

It is believed that the amendments to claim 516 and 524 are supported by Applicants' disclosure. Moreover, these amendments are believed to patentably distinguish Applicants' claimed invention from any of the cited documents, including Maniatis's Molecular Cloning (1982) publication.

4. ***New Claims 548 & 549***

Commensurate with Applicants' disclosure as just described in Point 3 above, new claims 548 and 549 have been added to further define the repeating low-complexity polynucleotide sequence of a dinucleotide repeat or a trinucleotide repeat. In both of claims 548 and 549, such dinucleotide repeat is "selected from selected from the group consisting of poly dGT, poly dAC, poly dCT, poly dAT, poly GC and poly dGA." Further, the trinucleotide repeat is "selected from the group consisting of poly dGAT and poly dGTA." The dinucleotide repeats recited in new claims 548 and 549 include the six members which are disclosed in original claim 78 (poly dGT, poly dAC, poly dCT, poly dAT, poly dGC and poly dGA). The

two trinucleotide repeats recited in both new claims include the two members disclosed on page 15 (poly deoxy GAT and poly deoxy GTA).

III. Other Matters

A. Claim 520 (& DNA derived from a filamentous phage)

As indicated above in Point C to the "Summary of the August 12, 2004 PTO Interview," footnote 2 on page 83 in Applicants' May 28, 2004 Amendment states:

> See the original specification, page 16, lines 11-20; Example 32; and original claims 31, 32, 44, 45, 70 and 71 (DNA polymer or bridging entity "is *derived* from a filamentous phage").

The portions and claims listed above in footnote 2 would appear to provide the requisite support required for the language in present claims 520 and 523 regarding the DNA molecule being derived from a filamentous phage.

B. Claim 506

Applicants respectfully continue to maintain that the cited Langer et al. document does not disclose a polynucleotide sequence covalently attached to an antibody. As indicated in Applicants' May 28, 2004 Amendment, Langer et al. disclose a biotin molecule covalently attached to a DNA molecule and an antibody that is noncovalently attached to the previously attached biotin molecule. In other words, in the cited Langer et al. document, biotin is *not* covalently attached to an antibody. Biotin binds *non-covalently* to avidin.[5] Biotin and avidin bind to each

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[5] *See* Langer et al, US Patent No. 4,711,955, col. 1, lines 44-47, col. 18, lines 19-21, previously cited of record in this application; see also Laitinen et al., "Chicken avidin-related proteins show altered biotin-binding and physico-chemical properties as compared with avidin," Biochem J. 363:609-17 (2002); see in particular the abstract on page 609. A copy of Laitinen et al. was attached as Exhibit 1 to Applicants' May 28, 2004 Amendment.

other via ionic, polar and/or hydrogen bonds.[6] Because a non-covalent bond is always interposed between biotin and any antibody attached to avidin, the indirect attachment of biotin to the antibody on avidin cannot be characterized as covalent. As such, the antibody in Langer et al. cannot reasonably be construed to be covalently attached to a polynucleotide sequence as set forth in claim 506. Thus, Langer et al. lack a material element recited in claim 506, namely, an antibody that is covalently attached to a polynucleotide sequence.

Although they believe the foregoing information is sufficient to dispose of the anticipation rejection of claim 506 by Langer et al., Applicants are exploring the possibility of submitting further evidence on this matter. If and when such evidence becomes available, their attorney will submit it promptly to the Examiner for his consideration and review as it might relate to the patentability of claim 506.

Favorable action on this application is respectfully requested.

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[6] *See* Weber et al., "Structural Origins of High-Affinity Biotin Binding to Streptavidin," Science 243:85-88 (1989). A copy of Weber et al. was attached to Applicants' May 28, 2004 Amendment as Exhibit 2.

SUMMARY

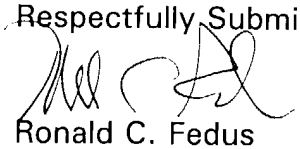
This paper follows the August 12, 2004 PTO interview.

Amended in this paper are claims 509, 516, 522 and 524. Canceled are claims 509, 512-515 and 526. New claims 548 and 549 have been added. Thus, as set forth in the complete listing of the claims provided above, the pending claims in this application include 283-362, 364-380, 382-398, 400-404, 406-439 and 441-508, 510-511, 516-525 and 527-549.

In light of the cancellation of six claims and the addition of two new claims, no fee is believed due in connection with the filing of this Amendment. If any fee is due, however, The Patent and Trademark Office is hereby authorized to charge the amount of any such fee to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If the Examiner has any questions, he is invited to contact the undersigned attorneys.

Respectfully Submitted



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